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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/03/2003

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/734,672	MURPHY ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed on 03/24/03 has been acknowledged.

Claims 28-48 are pending and are examined in this office action.

► *Applicants are advised to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). Each amendment document that includes a change to an existing claim, or submission of a new claim,* ***must include a complete listing of all claims*** *in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

Election/Restrictions

1. Applicant's election with traverse of Group II (claims 28-48 **wherein the elected nucleic acid sequences is SEQ ID NO:3, which encodes the amino acid sequences of SEQ ID NO:4, BRCA1omi2)** in Paper No. 15 is acknowledged. The traversal is on the ground(s) that both SEQ ID NO:1 and 3 contains recited thymidine substitution at position corresponding to nucleotide 2201 and therefore are not structurally different. The applicant argues that these sequences are not involved in breast cancer therefore have same function. The applicant concluded that there is no serious search burden since both nucleotide sequences contain same substitution and search or either sequence will reveal nucleic acid present in the prior art. This is not found persuasive because SEQ ID NO:1 and SEQ ID NO:3 are structurally distinct nucleotide sequences, wherein the mutations in one does not matches with other. In addition the burden of search exists, since a different search is required for each separate PS site, haplotype and nucleic acid molecules. For example, in order to properly search a substitution at position 2201 of SEQ ID NO:1, this haplotype will need to be searched separately in the computer database maintained by the STIC

along with individualized searching of polymorphism, mutations and/or haplotypes in commercial databases. Review of this information would be different for each PS site, haplotype in each nucleic acid molecule, and would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claim 28-48 are objected to because of the following informalities: The instant claims encompasses a non-elected subject matter SEQ ID NO:1 and SEQ ID NO:2 respectively. However the elected subject matter is isolated nucleic acid molecules of SEQ ID NO:3 which encodes the amino acid of SEQ ID NO:4. Appropriate correction is required.

3. Claim 28 is objected to because of the following informalities: The instant claim recites claim limitation "SEQ ID NO:1 and fragments thereof". Changing "SEQ ID NO:1 and fragments thereof" to "SEQ ID NO:1 or fragments thereof" has been suggested. Appropriate correction is required.

4. Claims 29-33 and 35-48 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In instant case SEQ ID NO: 1 and 3 are structurally distinct nucleotides, therefore the recitation of SEQ ID NO:3 in dependent claims does not further limit the base claim that requires the nucleotides of SEQ ID NO:1.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. For example, pages 2, 34 and 37 of instant application contains embedded hyperlink and/or other form of browser-executable code

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 28, 34 and 42-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of instant claims encompasses an isolated nucleic acid molecule that encodes a BRCA1 protein which contains a thymidine for cytidine substitution at position corresponding to nucleotide 2201 of SEQ ID NO:1 and fragments thereof containing the substitution. In addition

the scope of isolated nucleotide sequences as claimed encompasses a nucleic acid molecule that encodes a BRCA1 protein containing a serine residue at a position corresponding to amino acid 694 of SEQ ID NO:2. Given the broadest reasonable interpretation the invention the scope of invention as claimed encompasses any and all natural and non-natural variants of BRCA1 gene which contains a thymidine for cytidine substitution at position corresponding to the nucleotide 2201 of SEQ ID NO:1.

At best the instant specification only disclosed SEQ ID NO:1 and SEQ ID NO:5 which at position 2201 contains a thymidine. In addition the specification teaches the nucleotide sequences of SEQ ID NO:3, which at position 2201 contains a cytidine residue. Besides the nucleotide sequences of SEQ ID NO:1 and SEQ 5 the specification fails to disclose any other natural variant of BRCA1 that contains thymidine for cytidine substitution at position corresponding to nucleotide 2201.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol. 66, No. 4, pp. 1099-1100 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only disclosed SEQ ID NO:1 and SEQ ID NO:5 that encodes a BRCA1 gene and contains a thymidine at position 2201 (see sequence listing). Besides SEQ ID NO: 1 and 5 the specification fails to disclose any mutant or polymorphic form of BRCA1 gene that contains a thymidine for cytidine substitution

at position 2201 relative to SEQ ID NO:1 and has functional property of BRCA1 polypeptide explicitly or implicitly as putatively claimed by the applicant.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses BRCA1-like activity which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The invention as claimed only requires a thymidine for cytidine substitution at position 2201 in context with the nucleotide sequence of SEQ ID NO:1. The invention as claimed does not provides any structural limitation that distinguishes the claimed nucleic acid from any other nucleotide sequence that contains

thymidine for cytidine substitution. The state of art at the time of filing teaches that mutation in human BRCA1 gene confer a high risk of breast and ovarian cancer. There are **over 878 distinct mutations**, polymorphisms and variants throughout the *BRCA1* gene, which are not limited to a particular region of the gene. Most mutations in BRCA1 gene are even considered private (see Breast Cancer Information Core http://www.nhgri.nih.gov). see Yassaee et al (Breast Cancer Res. 2002;4(4):R6. Epub 2002 Apr 16; (see page 2, col.1 para.3, page 5, table 1). Besides a thymidine for cytidine substitution at position 2201 the applicant fails to disclose what is the structure of BRCA1 variant as claimed which is structurally distinct from the nucleotides of SEQ ID NO:1 explicitly or implicitly. Given the broadest reasonable interpretation the invention as claimed reads upon a nucleotide sequence wherein any and all nucleotide sequences has been added, substituted or deleted (other than thymidine at position 2201) over the entire length of the proposed nucleotide sequence.

The variation as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus

because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

7. Claims 28-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature Of Invention:

Invention relates to BRCA1 mutations and polymorphism

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of instant claims encompasses an isolated nucleic acid molecule that encodes a BRCA1-like protein which contains a thymidine for cytidine substitution at position corresponding to nucleotide 2201 of SEQ ID NO:1 and fragments thereof containing the substitution. In addition the scope of isolated nucleotide sequences as claimed encompasses a nucleic acid molecule that encodes a BRCA1 protein containing a serine residue at a position corresponding to amino acid 694 of SEQ ID NO:2. Given the broadest reasonable interpretation the invention the scope of invention as claimed encompasses any and all natural and non-natural variants of BRCA1 gene which contains a thymidine for cytidine substitution at position corresponding to the nucleotide 2201 of SEQ ID NO:1. At best the instant specification only disclosed SEQ ID NO:1 and SEQ ID NO:5 which at position 2201 contains a thymidine (see sequence listing). In addition the specification teaches the nucleotide sequences of SEQ ID NO:3, which at position 2201 contains a cytidine residue. Besides the nucleotide sequences of

SEQ ID NO:1 and SEQ ID NO: 5 the specification fails to disclose any other natural variant of BRCA1 that contains thymidine for cytidine substitution at position corresponding to nucleotide 2201.

State Of Art And Predictability:

The state of art at the time of filing teaches that mutation in BRCA1 gene confer a high risk of breast and ovarian cancer. At present, there are over 878 distinct mutations, polymorphisms and variants throughout the *BRCA1* gene, which are not limited to a particular region of the gene. Most mutations in BRCA1 gene are considered private (see Breast Cancer Information Core http://www.nhgri.nih.gov). Identification of novel mutations in a particular population further suggests the need for developing a mutation data-base for a given population. Yassaee et al (Breast Cancer Res. 2002;4(4):R6. Epub 2002 Apr 16; (see page 2, col.1 para.3, page 5, table 1). The state of art a the time of filing teaches that despite intensive investigation in the field of mutation detection technology, several problems still hamper the mutational screening of members of families at high risk for breast or ovarian cancer. The very large coding regions of *BRCA1* (5 kb) and the wide spectrum of mutations make screening laborious and inevitably decrease the reliability of the result whatever the mutation detection method used. Furthermore, most of the PCR-based methods, including genomic double strand sequencing, miss regulatory mutations and major genomic rearrangements that can occur quite frequently in specific populations. In addition, non-technical drawback is related to the genetic heterogeneity of the disease itself, besides *TP53*, *PTEN* and *ATM* genes, which are responsible for hereditary syndromes that also include breast cancer among the disease phenotypes, the presence of dominant loci other than *BRCA1* is very likely. Montagna et al Int J Cancer. 2002 Apr

10;98(5):732-6. see page 734, col.2 para.3, table-1). Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore considering the limited amount of guidance provided in the instant specification and the state of BRCA1 mutation art it would require undue amount of experimentation to identify various mutants, polymorphic forms and variants wherein besides other sequence variations the nucleotide as claimed contains thymidine for cytidine substitution at position 2201 in view of SEQ ID NO:1.

Quantity Of Experimentation Required:

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In instant case screening of any and all natural and non-natural variants of BRCA1 gene over the entire length for any and all mutations is not considered routine. Besides a thymidine for cytidine substitution at position 2201 the applicant fails to disclose what is the structure of BRCA1 variant as claimed which is structurally distinct from the nucleotides of SEQ ID NO:1 explicitly or implicitly. Given the broadest reasonable interpretation the invention as claimed reads upon a nucleotide sequence wherein any and all nucleotide sequences has been added, substituted or deleted (other than thymidine at position 2201) over the entire length of the proposed nucleotide sequence. Making and testing a point mutation in a know nucleotide sequence is significantly different from the making and testing a

sequence of unknown structure and function wherein any and all nucleotide sequences has been added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed BRCA1 activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

8. Claims 44-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell and/or method of producing a polypeptide by an isolated host, does not reasonably provide enablement for a host cell and/or method of producing the polypeptide, wherein the host cell is in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature Of Invention:

Invention relates to method of gene therapy or transgenic animals.

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of invention as claimed relates to a recombinant host cell and/or a method of producing recombinant proteins from the host cell, wherein the host cell is in-vivo.

State Of Art And Predictability:

The art at the time of filing clearly teaches that the Gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations. It has been difficult to predict the efficiency and out come of transduced genes because various factors govern the expression and/or therapeutic potential of transduced genes in vivo. The transduction of target cells represents the first critical step in gene therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. Although the retroviral vectors are the vectors of choice, they require target cells to be in cycling state for the successful delivery of gene of interest. On the other hand vector comprising DNA viruses and liposome coated DNA have been used to transduce non dividing cells but this results in a transient expression due to non-integration of transgenes in host cells. In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacles to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets (see Rosenberg et al, Science 287:1751, 2000, Anderson WF, Nature 392:25-30, 1998; Verma et al Nature 389:239-242, 1997). In instant case the invention as claimed reads upon any and all types (skin, muscle or blood cells etc) recombinant host cell in vivo, wherein the cell expresses the claimed BRCA1-varinat. The state of art at the time of filing teaches that BRCA1 gene has been associated with

high risk of breast and ovarian cancer (supra). The only disclose utility of a recombinant host cell (in-vivo) expressing the BRCA1-gene is in-vivo gene therapy (spec. page 21-23). The specification fails to disclose any recombinant cell produced in vivo would ameliorate the breast or ovarian cancer in any subject.

Similarly, the state of transgenic art at the time of filing was such that phenotype of an animal is determined by a complex interaction of genetics and environment. Many biochemical pathways are plastic in nature, which reflects the ability of the embryo to use alternative gene when the preferred gene is modified. It is known in the art that the level and the specificity of a transgene as well as the phenotype of the transgenic animal are greatly dependent upon the specific expression vector used. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, for example are the important factors that govern the expression of a transgene (see Wood. Comp. Med. 50(1): 12-15, 2000, Wall RJ Theriogenology 45:57-68, 1996, Kappel et al. Current Opinion in Biotechnology 3:558-553 1992) In instant case the specification as filed fails to disclose a single transgenic animal that contains a host cell encoding the claimed BRCA1-gene, wherein the transgenic host cell in vivo produces the claimed gene product.

Quantity Of Experimentation Required:

In instant case making a host cell to produce recombinant protein (in-vivo), wherein the host cells is created by a method of gene therapy or a method of making transgenic animal are not considered routine in the art and without sufficient guidance the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular

area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. Amending the instant claims to limit the invention to an isolated host cell would obviate this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim 28 recite claim limitation "corresponding nucleotide 2201 of SEQ ID NO:1" in line 2. Changing "corresponding nucleotide 2201 of SEQ ID NO:1" to "corresponding to nucleotide 2201 of SEQ ID NO:1" has been suggested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 28, 34, 42-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Shattuck-Eidens et al (US 5,693,473, 1997, filed 06/07/1995).

Shattuck-Eidens et al teaches an isolated nucleic acid sequence that encodes BRCA1 protein, which contains thymidine for cytidine substitution at a position 2201. The cited art further teaches an isolated nucleic acid molecule that encodes a BRCA1 protein containg a serine residue at position 694 (see col.9, line 11). In addition the cited art teaches a vector comprising the BRCA1 gene, a prokaryotic or eukaryotic host cell and method of producing the polypeptide by culturing the host cells (see col. 26, lines 10-68, col.27 lines 1-57, col.32 line 24). Thus the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or

proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

SUMESH KAUSHAL
PATENT EXAMINER